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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/586,131	06/02/00	DELCOURT M	1184-00

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EXAMINER	
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ART UNIT	PAPER NUMBER
1627	8

DATE MAILED: 04/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Offic Action Summary	Application No.	Applicant(s)	
	09/586,131	DELCOURT, MARC	
	Examiner	Art Unit	
	Thomas W Prasthofer	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☒ Claim(s) *1-19* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

Detailed Action

Status of the Application

Receipt is acknowledged of a response to a restriction requirement on April 12, 2001 (Paper No. 7).

Status of the Claims

Claims 1-20 were pending in the present application. Claim 20 is withdrawn from consideration by the Examiner as being drawn to a non-elected invention. Claims 1-19 are being examined on their merits.

Response to Restriction and Election of Species with Traverse

Applicant's election of Group II, claims 16, 17, and 19, with traverse is acknowledged. In response to Applicant's arguments, Examiner withdraws the restriction requirement between Groups I, II, and III and will examine claims 1-19 on their merits.

Objections to the Claims

1. Claims 12 and 19 are objected to because of the following informalities: The sentences does not end with periods. Appropriate correction is required.

2. Claim 17 is objected to because of the following informalities: The number of the claim being limited is missing. Appropriate correction is required.

3. Claims 1-19 are objected to because of the following informalities: Claims 1, 8, 17, and 18 are drawn to processes while the remaining dependent and independent claims are drawn to methods. Appropriate correction is required.

4. Claim 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The further steps recited in claim 11 do not further limit the process of claim 1 but expand on the process. Cleaving, purifying, and sequencing of the fragment are not a part of a process for isolating an intact clone. The added steps expand what is accomplished by the process of claim 1 by providing for the identification and/or characterization of the isolated clone.

Claims Rejections – 35 U.S.C. 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-19 are rejected under 35 U.S.C. 101 because the claimed processes (methods) are not supported by either a specific and/or substantial asserted utility or a well established utility.

The instant specification discloses that the claimed methods are useful for screening for finding sequences with enzymatic activity or homology to other sequences which can then be isolated, sequenced, transfected etc.; e.g. see page 1 and abstract.

Applicant's claimed method must satisfy 35 USC 101 and 112 (1) as defined by the statute and case law. In this regard, Applicant is directed to MPEP 2107; 2107.01 and 210.02 which provide guidelines for determining the criteria for satisfying utility and enablement.

Initially it is noted that merely disclosing the ability to make (or isolate) a compound or compounds (e.g. a library) is in itself insufficient utility to satisfy either 35 USC 101 or 112, first paragraph as determined by the U.S. Supreme Court. . Eg. See *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966).

According to the text of 35 USC sec. 101, an invention must be "useful". Our reviewing courts have applied the labels, "specific utility" (or "practical utility") to refer to this aspect of the "useful invention" requirement of sec. 101. (Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881,

883 (CCPA 1980)). In Nelson, the court characterized "specific utility" (or "practical utility") as "a shorthand way of attributing real-world value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." (Id. at 856.) With respect to the issue of pharmaceutical utility and **vague assertions** of biological activity, Applicant is further directed to *In re Kirk*, 376 F.2d 936, 941, 153 USPQ 48, 52 (CCPA 1967)) and *Cross v. Iizuka*, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), wherein the Federal Circuit labeled Applicant's assertion of "biological activity" without more specifics as a "nebulous" expression. Such statements, the court held, "convey little explicit indication regarding the utility of a compound" and do not satisfy either the utility and/or the enablement statutory requirements.

The claimed methods for isolating an intact clone of a target nucleic acid are not supported by a specific asserted utility and do not, without further research and experimentation, provide an immediate benefit to the public. Rather, the claimed method isolates target nucleic acid sequences so that they may be "studied" (instant specification, page 3, first paragraph). Any benefit to the public (to one of ordinary skill in the art) is speculative. The breadth of the claims includes literally any fragment of DNA from any organism or produced by any synthetic means. The DNA fragment isolated using the claimed method has "a known characteristic" which may be any characteristic whatsoever. Given the breadth of the claims, it is certain that some intact clone of one target nucleic acid fragment having a known characteristic will be found. What that characteristic is and the identity of the fragment are left for one using the invention to determine. Therefore the specific and substantial utility of the invention is left for the user of the invention to determine. Note, because the claimed invention is not supported by a specific asserted utility for the reasons just set forth, credibility cannot be assessed.

This is not to say that inventions that are to be used exclusively in a research setting (i.e., research tools) always lack a specific asserted utility. Indeed, many research tools such as telescopes, gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility. (See USPTO Utility Guidelines, page 12.)

However, inventions that have a specifically identified utility must be distinguished from those whose utility requires further research to identify or reasonably confirm. Research tools (such as gas chromatographs, screening assays, etc.) are useful in the sense that they can be used

in conjunction with other method steps to evaluate materials other than themselves or to arrive at some result. The claimed methods are not research tools in this sense. Rather, they are themselves the subject of basic research, whose usefulness or lack thereof has yet to be established.

In the absence of an asserted specific utility, the "useful" requirement may be established by reference to a well established utility. A "well established utility" is a "specific utility" which is well known, immediately apparent and implied by the specification based on the disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

The claimed methods are not supported by a well established utility, however, because neither the specification as filed nor any art of record discloses or suggests any property or activity for the DNA fragments to be isolated such that another non-asserted utility would be well established for the compounds.

Given the universal breadth of the claims with regard to nucleic acid fragments and their characteristics and the lack of even a single example in the specification of a specific sequence or characteristic, the burden of undue experimentation is placed on the public to determine the utility of the invention.

Claims Rejections – 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-19 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

7. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Undue experimentation would be required to use the claimed invention.

Several factors are to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any required experimentation is "undue." These factors include:

1) the breadth of the claims
2) the nature of the invention
3) the state of the prior art
4) the level of one of ordinary skill
5) the level of predictability in the art
6) the amount of direction provided by the inventor
7) the existence of working examples
8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The breadth of the claims is universal with regard to the nucleic acid fragments and associated characteristics encompassed by the claims. The fragments can be cDNA, genomic DNA, mitochondrial DNA, DNA derived form nature (from any organism), or synthetic DNA. The fragments may encode any protein or RNA or be homologous to any other nucleic acid. All methods of screening for a characteristic of a nucleic acid fragment and/or its expression products are encompassed by the claims. These include Northern, Southern, and Western blots, ELISA, phage display and panning, binding assays, etc.

The nature of the invention is a method for isolating an intact clone of one target nucleic acid fragment with a known characteristic from a group of fragments. The method involves restriction digests of cloned fragments to generate monodigested libraries that are screened for a known characteristic. The known characteristic will be present or absent depending on the whether the restriction enzyme used cleaves the fragment in such a way as to interfere with the known characteristic. The enzymes that do not interfere with the known characteristic are then

used to cleave the source of the fragments to produce a multidigested library having an intact clone of the target nucleic acid fragment.

The level of predictability in the art is low for circumstances in which the nucleic acid fragments and associated characteristics are not known. It is not possible to predict the outcome of screening, cloning, and restriction fragmentation when the characteristic being screened for and the nature of the nature and source of the nucleic acid are not specified in any way.

The amount of direction provided by the inventor is not adequate to enable one of ordinary skill in the art to use the claimed invention. No guidance as to nucleic acid selection, methods of screening, or characteristics to screen for is provided.

No working examples are provided to illustrate the use of the claimed method. Example 1: Preparation and exploitation of an expression library provides lists of potential expression products to be screened and a variety of possible screening techniques. The example provides COS cells as a potential cell line to be used for transfection of mammalian cells. Example 2: Cloning by homology provides no guidance with respect to characteristics to screen for, or homologies to be screened for or the sources of nucleic acid fragments. Example 3: Southern blot "Identiblot" identification provides no guidance with respect to target fragments of nucleic acids or identities to screen for. Similarly, examples 4-6 provide no guidance except for a reference to the use of DNA chips that are "useful for the examination of the gp120 of the HIV virus or cellular oncogenes such as p53."

The quantity of experimentation needed to make or use the invention based on the content of the disclosure is great. One using the invention must determine the characteristic to be screened for, the method(s) of screening, select a source(s) of target nucleic acid fragments, and make a cloning or cloning/expression vector that lacks restriction sites for 10 –70 different restriction enzymes and 3-4 other known restriction enzymes. Depending on the desired characteristics and nucleic acid fragments, expression vectors in bacteria, yeast, insects, plants, or animal cells or gene knockouts in mice or other animals or plants may be required to screen for the desired property.

For the reasons provided, undue experimentation would be required of one of ordinary skill in the art to use the claimed invention.

Claims Rejections – 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 2, 5, 6, 9, and 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite the limitation "the method" in the preamble. There is insufficient antecedent basis for this limitation in the claim.

9. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting an essential step, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step is: isolating an intact clone from the library. The preamble of the claim recites a process for isolating an intact clone but the method steps result in a library of clones rather than an isolated intact clone. Not that dependent claim 10 provides the missing essential step and that it should be cancelled if the independent claim is amended to include that step.

10. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear how a "group of fragments" can contain 1 fragment as recited in the range "from 1 to 108 fragments."

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Thomas Prasthofer** at telephone number **(703) 308-4548**. The examiner can normally be reached on Monday-Friday, 8:00-4:30.

12. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-2742.

13. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist at (703) 308-1235.

Thomas Prasthofer, Ph.D.
4/20/01

BENNETT CELSA
PRIMARY EXAMINER
4/20/01